Extra-Cellular Matrix Fabrication Method Utilizing ECM-Associated Antigens for in-Vitro Organ Generation in the Absence of Existing ECM, Applications for Curing Paralysis

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Introduction

A variety of tissues in the human body, bacteria, virii, and abnormal cells such as cancer cells have been found to secrete antigens that can be detected and used to, for example, detect the presence of cancer in the context of a blood test or, in the case of the immune system, forms the impetus for natural immune system reactions.

Abstract

Inspired by a phenomenon I discovered while trying to eliminate a patch of dermatitis, I have come to the conclusion that all tissues in the human body have an ECM-associated antigen signature. While it is already understood that all tissues have an ECM, it is not yet understood that each localized section of ECM has a unique location-specific signature. These signatures, I found, are agnostic to the left versus the right side of the body since the organ systems on each side are essentially mirrors of one another.

A healthy, normally-functioning immune system will not attack tissues based upon these hypothesized ECM-associated antigens (ECMAAs,) however, individuals with autoimmune disorders such as eczema, psoriasis, lupus, etc. will experience the symptoms associated with the immune system targeting these antigens.

Supporting this theory, I found that treating a patch of dermatitis localized on a certain part of one limb of the body using a commonly-prescribed topical corticosteroid resulted first in an abatement of symptoms in the affected area but with great regularity also resulted in the eruption of symptoms on the same part of the opposite limb just days or weeks later.

I hypothesized that the cause of this phenomenon was the predisposition of the immune system to attack tissues saturated with a specific antigen common to that section of the dermis; an antigen present, naturally, in identical sections opposing limbs. If each section of dermis has its own specific antigen signature duplicated only in the corresponding section of the opposite limb, it would explain why the immune system would attack one side only and then attack the exact opposite side when precluded by the steroid from attacking the original site.

Using this premise as a starting point, I took a look at the technical challenges involved in curing paralysis. More challenging than coaxing two existing sections of spinal cord to reconnect is bridging the gap in spinal tissue in cases where, as in most cases, centimeters or even several inches of cord tissue may be missing. To treat this condition, a new length of cord bundle

must be re-grown and installed. There is still an open debate as to whether the best solution would be some sort of electronic relays to bridge the gap, an in-vivo growth solution, or perhaps an in-vitro partial organ replacement and subsequent installation.

Considering the challenges and limitations of each potential cure avenue, I believe that the technical challenges involved in the in-vitro growth of spinal tissue (as well as other organ systems where ECM is either corrupted or not accessible) may be overcome using the method I propose herein. Natural spinal tissue implanted and re-attached will restore the greatest degree of function to paralysis victims as opposed to other approaches.

Existing techniques that depend upon washing away corrupted cells leaving only ECM and using iPS to regrow immune-compatible cells atop that structure require having an ECM scaffold to work with in the first place. When it comes to kidneys, livers, and even hearts, it is possible to use the existing method to grow a biologically new, "perfect" organ. When it comes to the spinal cord (and other organs as well if the ECM is corrupted) the absence of part of the ECM and the delicacy of the spinal cord makes removal of the remaining sections of cord and ex-vivo reconstruction implausible.

In most spinal cord injuries, only short sections of fiber are actually missing or the cord is only partially severed. Coaxing sections into re-attaching is actually the easy part once the length difference can be compensated for by replacing the missing length of tissue. The spinal cord does not readily tolerate having too much or too little "slack" in its length. Before the installation of any lab-grown spinal cord lengths, the existing cord would need to be surgically cut to create a freshly exposed fiber free of scar tissue. This step, though necessary, is also simple in comparison to the process of growing spinal tissue in-vitro.

To understand how it may be possible to grow lengths of spinal cord in-vitro, one has to understand what it is that ECM is actually doing to guide iPS cell transformations in the first place. That's where the ECMAAs come into play. Not only do ECMAAs provoke immune responses (potentially) in those with immune disorders that cause tissues to be attacked, but these same as-yet undiscovered antigens are what provide instructions to iPS cells as to what cells they should become. Under the right conditions, these antigens can also instruct iPS to form into the ECM itself; a critical first step in artificial organ construction.

I propose that by mapping the unique signature of ECMAAs for each tissue of the human body (and furthermore tailoring that database to be bio-compatible with the immune system of specific individuals to prevent Graft Versus Host Syndrome) it would then be possible to create any desired organ system without a pre-existing ECM by doping iPS with the appropriate antigens to trigger the desired tissue conversion in each specific area.

Another crucial element is knowing under what conditions a new kidney cell, for instance, will become an ECM cell or some other component of a kidney. To understand this, one must know whether, for instance, an entire ECM forms during fetal development before more general tissues or if general

tissues form and then later solidify into ECM. After all, just because ECM bears some functional resemblance to the frame of a building does not mean its own mode of construction follows the pattern of a building's.

It would appear to this author that ECM actually forms subsequent to initial organ differentiation during fetal development as a result of a particular combination of conditions, sc. slightly decreased oxygenation, increased presence of calcium carbonate, and higher proportions of tissue-specific antigen in the localized area as opposed to in the elsewheres of the budding organ. During initial organ formation, antigen concentration is uniform and the ECM does not exist. The ECM begins to take shape, I submit, somewhat after the initial formation of the organ buds ultimately as a result of the accumulation of these antigens in greater quantities along branch-like lines near the center of the new organ. Once again, just because these fibers resemble tree branches does not mean they formed the way a tree branch forms.

Conclusion

Proceeding on this basis, it is reasonable to conclude that synthetic antigens can be constructed that are tailored to the individual in need of replacement organs with hundreds of unique antigens needed to inform the development of any organ system in-vitro. Mapping the full spectrum of ECMAAs in one individual or a variety of individuals will pave the way for a standard method to be developed that allows for those baseline antigen RNAs to be modified from the baseline to be bio-compatible with any given intended organ recipient.